# Tobacco and Health

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## New Study Points to Pollution Of Air as Lung Cancer Factor

A new scientific study published in the *British Medical Journal* presents findings that "suggest that the air pollution which occurs in modern industrial life—smoke, smog, traffic fumes, etc.—may be a major factor responsible for the alarming increase of lung cancer in South Africa and Britain, and presumably elsewhere."

The report* by Dr. Geoffrey Dean found that "white male South Africans have long been the heaviest cigarette smokers in the world, and yet they have a relatively low lung cancer mortality rate."

The study is based on 1947-56 male lung cancer deaths in the Union of South Africa by age, country of birth and place of residence. It showed that British immigrants to South Africa had much higher lung cancer mortality rates than Union-born men or immigrants from other countries.

Dr. Dean is senior honorary physician at Provincial Hospital, Port Elizabeth, South Africa. His findings are similar to a report**, to which he refers, by Dr. David F. Eastcott, assistant director of New Zealand's National Health Institute. Dr. Eastcott also found that immigrants from the United Kingdom had a higher incidence of lung cancer than native-born persons of the same stock and that differences in tobacco smoking did not appear to be involved.

In his study, Dr. Dean noted that British male immigrants to South Africa who died between the ages of 45 and 64 had a much higher lung cancer rate than either white native-born men or male immigrants from other countries for the same age groups.

"As most of the British immigrants came to South Africa before reaching middle age, British cigarettes are likely to have formed only a small percentage of the total cigarettes smoked by those dying of lung cancer at these ages," he said.

"It is therefore unlikely that the difference in lung cancer mortality experience in these age groups is at-

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* "Lung cancer among white South Africans." *British Medical Journal*, October 31, 1959.
** "The epidemiology of lung cancer in New Zealand." *The Lancet*, January 7, 1956.

## Chest Specialist Sets Forth Views On Lung Cancer

The increased incidence of lung cancer is indicative of improved diagnostic techniques and longevity, writes Dr. Milton B. Rosenblatt, associate professor of medicine at New York Medical College and co-author of a medical text on lung cancer.

Dr. Rosenblatt said* explanations for the increased prevalence of lung cancer have included such etiologic possibilities as inhalant carcinogens from automobile exhausts and industrial combustion motors, tarring of roads, inflammatory metaplasia from antecedent bronchopulmonary infection, occupational exposure to asbestos, silica and chromium, and smoking.

"In general, the inhalation theories have not stood the test of time," he said.

Dr. Rosenblatt, co-author of "Cancer of the Lung," published by Oxford University Press, said that dissenting opinions in regard "to the potentialities of smoking as a cause of lung cancer" may be summarized as follows:

"1. Cancer of the lung has been an established entity in the medical literature for 150 years,

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*"Bronchogenic Carcinoma: Etiologic considerations." *Clinical Medicine*, Vol. 6, pages 959-969, June 1959.

## New Evidence Cited In Comments on PHS Smoking Review

Accumulating scientific evidence "that conflicts with or fails to support the tobacco-smoking theories of lung cancer" was recently cited by Dr. Clarence Cook Little, cancer research scientist who is Scientific Director of the Tobacco Industry Research Committee.

Dr. Little's statement was made upon publication in the November 28 issue of the *Journal of the American Medical Association* of a review entitled "Smoking and Lung Cancer," by the United States Public Health Service (PHS).

He said that many of the recent scientific reports on smoking and lung cancer were either "omitted from or glossed over" in the PHS review.

"Despite these recent research trends," said Dr. Little's statement, "the conclusions set forth in the review rely almost entirely on past re-

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## No Lung Cancer in 5 Years of Tests With Tobacco and Animals

Five years of tests in which large numbers of animals were exposed to "strong concentrations" of cigarette smoke have failed to produce a single lung cancer, says the latest report of the British Empire Cancer Campaign.

The 36th Annual Report of the world-wide cancer effort described the experimental work done under Dr. R. D. Passey at the Institute of Cancer Research, Royal Cancer Hospital, London, England.

"The lack of success of many experiments with cigarette smoke and its products to throw light on the problem of the association of lung cancer with cigarette smoking has led to the suggestion that the associa-

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## Study Cites Air Pollution As Lung Cancer Factor

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tributable to differences between South African and British cigarettes; and this would seem to be broadly confirmed by the fact that the lung cancer mortality rate in the U.S.A. is much lower than the rate in Britain, though the same type of tobacco formed the basis of cigarettes in both countries.

"The excess lung cancer mortality among British male immigrants, as compared with Union-born white men, is found only in those dying of lung cancer under the age of 65," he said. "Above that age there is no significant difference between the lung cancer mortality rates in the two groups.

"This suggests, therefore, that the greater liability of the more recent British immigrants to lung cancer is a relatively new phenomenon, and that the immigrants were exposed to the etiological factor or factors concerned before they left Britain.

"The higher incidence of lung cancer among residents in South African towns . . . as compared with the incidence among residents in rural areas, would seem to be strong evidence that atmospheric pollution is an important factor," Dr. Dean said. "If so, it is equally likely that the higher incidence among the more recent British immigrants may again be connected with the atmospheric pollution to which they were exposed before emigrating.

"The relatively low incidence of lung cancer generally among the heavy-smoking South African men, the higher and rapidly increasing incidence in the growing cities, and the high incidence in the younger age group of immigrants from Britain found in the present study, suggest that the air pollution which occurs in modern industrial life—smoke, smog, traffic fumes, etc.—may be a major factor responsible for the alarming increase of lung cancer in South Africa and Britain, and presumably elsewhere," he said.

"It is interesting to note," he wrote, "that most of the British immigrants came from cities rather than from the rural area in Britain. It should also be added that many of the patients, Union-born and immigrant, who died from lung cancer had suffered from recurrent bronchitis."

Among all three categories in South Africa — Union-born, British male immigrants and male immigrants from other countries—the lung cancer mortality rates have increased approximately with the level of urbanization and industrialization, he said.

"Neither the differences between the lung cancer mortality rates of these three groups nor the urban/rural gradient can be attributed to differences in smoking habits," Dr. Dean said. "Instead, both would seem to have been due to the exposure of the men concerned to different degrees of atmospheric pollution."

## Chest Specialist Gives Views on Lung Cancer

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antedating the era of cigarette smoking by a century.

"2. In institutions with routine autopsies and awareness of the disease there has been no real increase in the ratio of lung cancer to total cancers.

"3. The current difficulties in the diagnosis of bronchogenic carcinoma suggest that a percentage of the huge respiratory death rate in the early part of this century may well have been due to lung cancer. If this diagnostic error is estimated as low as 5 percent, the death rate from lung cancer at the turn of the century would have been as great as it is today.

"4. The validity of the statistical conclusions has been challenged on the basis of improper selection of controls, lack of autopsy confirmation of the cause of death and lack of correlation between the death rates of the heavy smokers in the survey as compared with the death rates for the total white male population of the United States.

"5. The relationship between induction of skin cancer in susceptible strains of mice and bronchogenic carcinoma remains to be established. Experienced investigators have found tobacco tar condensate to be a very weak carcinogenic agent in comparison with many other substances. The perpetual tobacco staining of fingers of heavy smokers have produced no increase in the incidence of cancer of the skin. The experimental exposure of mice to tobacco smoke for long periods of time did not produce lung cancer. Bronchogenic carcinoma has never been produced in the experimental animal by the use of tobacco or tobacco products."

Dr. Rosenblatt said that before the statistical evidence can be accepted as establishing a causal relationship between smoking and lung cancer, it must be determined whether the rise in incidence is real or apparent.

"There is considerable evidence that the epidemic-like increase is due to factors totally unrelated to cigarette consumption," he said. "These factors are the development of better diagnostic facilities and longevity of the population."

Dr. Rosenblatt wrote that it has repeatedly been pointed out that whenever an inaccessible cancer becomes accessible, "the incidence automatically increases."

He said conditions formerly considered as tuberculosis, unresolved pneumonia or non-specific inflammatory disease have since been correctly diagnosed.

As an instance, he cited the 10-fold increase in incidence of bronchial adenoma between 1940 and 1950, reported by R. L. McBurney and others in 1953.

"There is no question that the reason for this increase was improved diagnostic facilities," Dr. Rosenblatt said. "Inasmuch as bronchial adenoma arises from the submucous glands rather than from the epithelial surface, the increased incidence could not possibly have resulted from exposure to inhalant carcinogens."

***Tobacco and Health***

This publication periodically reports on scientific studies selected for broad interest and relevance to questions raised about tobacco use. No effort is made to include repetitive charges against tobacco that receive widespread publicity. This recognizes that other publications sometimes overlook studies and opinions that are at variance with the charges against tobacco. It is hoped that this information will help toward a balanced consideration of all aspects of tobacco and health questions.

Tobacco and Health
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# Statistics on Tobacco and Health Covered in Two Discussions

## Pleads for 'Integrity'

Present data on smoking and lung cancer are "logically incompetent," says a statistician in a discussion of statistical studies claiming an association exists between the two.

Dr. Horace W. Norton, professor of statistical design and analysis, department of animal science, University of Illinois College of Agriculture, commented* on a paper written by Dr. E. Cuyler Hammond of the American Cancer Society.

Dr. Norton said Dr. Hammond's paper** "will probably help many to understand why the available data on smoking and lung cancer are logically incompetent. Unfortunately, there are two points to which criticism must be directed."

He then disagreed with Dr. Hammond's expressed doubts on a possible third factor related to both smoking and lung cancer, and on a possible genetic origin of cancer.

"There is no need whatever to assume the recent appearance and rapid spread of such a genetic factor," he said. "Instead, it may have been widespread in human populations for eons. In particular, a genetic tendency to lung cancer would be under very slight selection pressure so long as it rarely affects individuals of reproductive age."

He then quoted Sir Ronald Fisher, noted English statistician, as providing evidence, which he says was not mentioned by Dr. Hammond, either in text or footnote, "to inform the reader that there is now a showing, beyond reasonable doubt, that the genotype has an important influence on choice of smoking habit."

In conclusion, Dr. Norton wrote: "I make a plea for integrity on the part of those affirming that smoking causes lung cancer. Let their various papers and public statements include (1) a frank acknowledgment that any such affirmative conclusion is a mere *opinion*, by no means fully substantiated by available data (this Hammond did) and (2) a familiar standard of comparison, choosing something over which we have, or ought to have, some voluntary control, such as the death rate associated with the use of the automobile."

## Not 'Necessary' Cause

The large number of smokers who do not have lung cancer "testify to the insufficiency of smoking as a cause of the disease," says a report* by two scientists.

Further, wrote Dr. J. Yerushalmy, School of Public Health, University of California at Berkeley, and Dr. Carroll E. Palmer, U. S. Public Health Service's Tuberculosis Program, "the existence of lung cancer patients who have never smoked clearly indicates that smoking is not a necessary cause."

They discussed statistical studies on smoking and lung cancer in an article on the methodology of investigations of etiologic factors in chronic diseases.

Discussing "multiple causation" factors in chronic diseases, they drew one example from the studies of smoking-lung cancer relationships, where "the immediate purpose is to determine whether smoking is implicated as a possible vector.

"If this were shown, further intensive analysis would be in order to determine how smoking causes the disease or what specific causative agent it contains," they said. "If such a specific agent were found, the demonstration that it causes lung cancer would not differ essentially in methodology from the demonstration that a certain microorganism causes a specific bacterial infection.

"It is likely that for many of the chronic conditions there may be more than one agent causing the disease, each of which may be found in more than one vector. Thus even if smoking is found to be a cause of lung cancer, it is obvious that the smoking *per se* is not the specific cause, but that tobacco smoke might contain the proximate causal agent.

"The same agent might be found in other environmental phenomena, such as automobile exhausts or fumes given off by various industrial processes. It is possible, also, that there are several different agents each of which may cause lung cancer and each of which may be found in one or more vectors. . . .

"To return to the smoking-lung cancer illustration, if smoking were shown to be related to lung cancer only or restricted to lung cancer and several related and physiologically explainable diseases, the association would have specificity and significance in suggesting a causal relationship.

"If, on the other hand, similar relationships can be shown with a variety of diseases, some of which cannot reasonably be thought to be influenced by smoking *per se*, then the association with cancer of the lung lacks specificity.

"The support which the statistical association provides for a causal relationship between smoking and lung cancer is correspondingly reduced."

* "Smoking and death rates—a riddle in cause and effect." Letter to editor, *American Scientist*, Vol. 47, pages 141-143, March 1959.

** *American Scientist*, Vol. 46, pages 331-354, Winter 1958.

* "On the methodology of investigations of etiologic factors in chronic diseases." *Journal of Chronic Diseases*, Vol. 10, pages 27-40, July 1959.

# Sir Ronald Fisher on Smoking-Lung Cancer

(Following is reprinted in its entirety from *Military Medicine*, July 1959.)

If you are one of those who has been convinced that there is a causal connection between smoking and lung cancer you should read *"Smoking—The Cancer Controversy."**

Sir Ronald Fisher, the author, is a man of many honors and many degrees; a statistician, by the way, who refutes the statistics which have been presented to convince us of that causal relationship.

States Sir Ronald: "My claim . . . is rather that excessive confidence that the solution has already been found is the main obstacle in the way of such more penetrating research as might eliminate some of them" (*possibilities*—italic ours).

This interesting little book will keep alive the controversy about the cause of lung cancer.

* *Smoking—The Cancer Controversy.* By Sir Ronald Fisher. Oliver & Boyd Ltd., Edinburgh. Price 2s.6d.

(Note: A limited number of copies of Sir Ronald Fisher's "Smoking — The Cancer Controversy" are available. Address requests to: The Editors, Tobacco and Health, 150 East 42nd Street, New York 17, N. Y.)



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## Cites New Data in Comments On PHS Smoking Review

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ports that are no more conclusive today than when these reports were first published.

"Most of the points are not new but are familiar to the American public because they were first advanced some years ago in statistical studies that admittedly are not supported by experimental evidence."

The PHS article was a review of papers published earlier. In the conclusions of the article signed by Surgeon General L. E. Burney, he stated his position as believing that "the weight of evidence, at present, implicates smoking as the principal etiological (causative) factor in the increased incidence of lung cancer."

The PHS conclusions also said that "cigarette smoking is particularly associated" with the alleged increase and that persons who stopped smoking or never smoked reduce their risk of lung cancer.

The PHS article also stated that "no method of treating tobacco or filtering the smoke has been demonstrated to be effective" in reducing lung cancer hazard.

These conclusions, Dr. Little's statement said, "place complete reliance on opinions published by those who are committed to the theory that tobacco has the principal causative role in lung cancer."

He pointed out that the review "clearly states that experimental evidence does not support the theories.

"The review recognizes that lung cancer afflicts non-smokers, and therefore can't all be blamed on smoking," he said. "It concedes the still-to-be evaluated role of air pollutants and occupational exposures. It admits differences in lung cancer incidence rates that cannot be explained by the smoking theory."

Dr. Little cited recent evidence that he said:

"1. Finds that people described as the world's heaviest cigarette smokers have low lung cancer death rates compared with people who smoke less but have been long exposed to urban air pollution.

"2. Shows that direct inhalation of tobacco smoke by laboratory animals over long periods of time has not resulted in causing lung cancer in these animals.

"3. Reveals that human lung tissues undergo changes, considered suspicious by some, that are found among both young and old, nonsmokers and smokers, while lung tissues 'may be perfectly normal in heavy smokers.'

"4. Confirms the long-established but little-publicized fact that lung cancer occurs more frequently in people who have a medical history of previous serious lung ailments, such as tuberculosis, pneumonia and influenza, indicating a relationship of possible significance."

(Note: Dr. Little's statement cited 23 scientific papers in support of these points. The full list and statement are available upon request to: The Editors, Tobacco and Health, 150 East 42nd Street, New York 17, N. Y.)

## Scientist Reports on Tobacco Insecticides

A team of agricultural research scientists has reported on studies indicating that the two major organic insecticides used on growing tobacco plants do not get into cigarette smoke at levels considered harmful to man.

The report* dealt with insecticides commonly known as TDE and endrin, and was on work done in the pesticide residue laboratory, Departments of Chemistry and Entomology, North Carolina State College, Raleigh.

In discussing the work done under his direction, Dr. Kenneth R. Keller, director of the college's tobacco research program, was quoted by the *Associated Press* as saying: "Even with the best available chemical techniques, it has not been possible to detect even traces of endrin from the smoke of an entire carton of cigarettes."

The levels of TDE traced in commercial cigarette smoke were more than four times less than the seven parts per million permitted on food by Federal regulation, the AP said.

The story quoted Dr. Keller as saying that a person would have to inhale, and retain, the smoke from a package of cigarettes a day for 250 years before he approached levels that might be considered harmful.

"Further research on chemical control has revealed that certain of the new experimental insecticides are heat degraded during flue-curing or smoking, resulting in an insecticide-free tobacco smoke," the AP said.

* "Insecticide Residues on Tobacco." T. G. Bowery, W. R. Evans, F. E. Guthrie and R. L. Rabb. *Journal of Agricultural and Food Chemistry*, Vol. 7, No. 10, October 1959.

## No Lung Cancer in Tests With Tobacco and Animals

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tion is an indirect one, and that some indirect approaches might lead to useful knowledge in this field," said Dr. Passey. "Several such approaches are being investigated at the moment.

"Our failure during the past five years (as recorded in previous Annual Reports) to induce lung tumors in mice, rats and hamsters by exposure to strong concentrations of cigarette smoke is a striking negative result," he said.

Dr. Passey reported that in the experiments the only lung cancer found was a solitary tumor in a control rat and "this tumor was associated with marked bronchiectasis.

"This has led to the careful examination of old breeding males, not subject to any smoking hazard, and six additional tumors have now been encountered in untreated animals," he said. "It is noteworthy that in each of these rats marked bronchiectasis has been an associated condition. The difficulty in the interpretation of this association is that, as in research institutes elsewhere, it is rare to make a post-mortem on any old rat without finding some more or less severe chronic bronchial lesions."

Sir Stanford Cade, head of the British cancer research effort, was quoted in news stories as saying that determining the exact relationship, if any, between smoking and lung cancer, was a "vexing problem" that required further research.

## No Lung Cancer In Canadian Arctic

"If smoking alone causes lung cancer, we should expect to find many cases in Eskimos and Indians, who almost all smoke quite heavily, mostly cigarettes in recent decades. No bronchogenic carcinoma has been found, however, in Northern natives by our x-ray survey teams, now regularly combing the Mackenzie district and the Eastern and Western Arctic, or in the Charles Camsell Hospital and Mountain sanatorium. While lung cancer has been found in Southern Indians, it is not known to exist in Northern Indians who had not yet any occasion to inhale much air polluted by car exhausts and industrial fumes. . . ."

("Medical observations and problems in the Canadian Arctic." Otto Schaefer, M.D., Edmonton, Alta. *Canadian Medical Association Journal*, Sept. 1, 1959.)



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